

In re Chang  
Appln. No. 09/837,217  
Amendmt. of June 1, 2004

## **REMARKS**

Claims 1-6, 8 and 11-14 are currently pending. Claims 1, 5 and 6 have been amended to point out more particularly and claim more distinctly the subject matter of the present invention. Applicant submits that no new matter has been added by way of this amendment.

In the Office Action of January 29, 2004, the Office set forth the following rejections:

- 1) claims 1-4, 11 and 13 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing new matter;
- 2) claims 1-6, 8 and 11-14 were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement;
- 3) claims 1-2, 11 and 13 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Moutsatsos et al. (WO 99/11664);
- 4) claims 1-2, 4, 11 and 13 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Riew et al. (Calcif. Tissue Int. 63:357-360, 1998), in view of Caplan et al. (U.S. 5,855,619); and
- 5) claims 1-2, 4, 11 and 13 are rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Cheng et al. (Calif. Tissue Int. 68:87-94, 2001), in view of Caplan et al.

These rejections are respectfully traversed for the reasons set forth below.

Reconsideration is respectfully requested.

### ***I. Rejections under 35 U.S.C. § 112, first paragraph***

The Office rejected claims 1-4, 11 and 13 under 35 U.S.C. § 112, first paragraph, for allegedly containing new matter. This rejection is respectfully traversed.

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Applicant has amended claim 1 in order to point out more particularly and claim more distinctly the subject matter of the present invention. In view of the amendment, it is clear that Applicant had possession of the claimed invention at the time the application was filed. See also, Office's Remarks, "Office Action of January 29, 2004," page 3, lines 1-4. As such, withdrawal of the rejection for new matter under 35 U.S.C. § 112, first paragraph, is respectfully requested.

The Office rejected claims 1-6, 8 and 11-14 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. This rejection is respectfully traversed. Applicant has amended claims 1, 5 and 6 to point out more particularly and claim more distinctly the subject matter of the present invention.

The Office argues that the specification does not reasonably provide enablement for a method of enhancing cartilage in a subject using the composition of the invention. Applicant respectfully submits that it was known in the art at the time of Applicant's invention that the expression of BMP-2 in pluripotent stem cells, including bone marrow stromal cells, can induce the cells to differentiate into cell types other than osteoblasts, e.g., cartilage and connective tissue. See, e.g., Moutsatsos et al. (WO 99/11664), at, for example, page 8, lines 16-22, and page 9, lines 5-12. In response, the Office argues that "example 1... is the only example... subsequent examples of Moutsatsos et al. only showed the formation of newly ectopic bone *in vivo*. "Office Action of January 29, 2004," page 10, second full paragraph.

In fact, Moutsatsos et al. describes several examples showing the expression of BMP-2 in pluripotent stem cells results in cartilage formation. Several of these examples are set forth in

Table 1:

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TABLE 1

Example	Result	Cell Line
Example 1	“C.9 transplants in the muscle developed into newly formed ectopic bone and cartilage.” Page 8, lines 16-17.	C3H10T1/2 cells (MSCs) infected with a retrovirus encoding $\beta$ -galactosidase, then infected with a viral vector encoding the cDNA for BMP-2.
Example 4	“Several implantations were completed which indicated that 10T overexpressing BMP-2 make cartilage and bone.” Page 11, lines 29-30.	10T cells (fibroblasts) transformed with DNA encoding BMP-2.
Example 11	“We observed a unique regeneration process which included well organized new growth of bone and cartilage within the boundaries of the fracture edges. In addition, a collar of differentiating and calcifying chondrocytes was formed around the original edge of the bone defect.” Page 26, lines 12-15.  “Following C3H-BMP2 transplantation, bone and cartilage formed around the fracture edge appeared organized and oriented according to the original pattern of radial bone, thus better reconstructing its original structure.” Page 27, lines 9-11.	C3H10T1/2 cells (MSCs) expressing rhBMP-2.
Example 15	“C3H10T1/2 cells expressing recombinant BMP-2 differentiate into chondroblasts and osteoblasts <i>in vitro</i> .” Page 50, lines 33-36.  “C3H10T1/2-BMP2: Day-20: Bony ossicle with hypertrophic cartilage (HC), bone (B) and bone marrow (BM). Sponge filled with proliferating cartilage.” Page 53, lines 5-9.	C3H10T1/2 cells (MSCs) expressing recombinant BMP-2

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Therefore, it is clear from at least Moutsatsos et al., that it was known in the art at the time of Applicant's invention that expression of BMP-2 in pluripotent stem cells, including bone marrow stromal cells, can induce the cells to differentiate into cell types other than osteoblasts, e.g., cartilage and connective tissue.

In view of the above, Applicant submits that claims 1-6, 8 and 11-14 are properly enabled by the specification as required by 35 U.S.C. § 112, first paragraph, and the withdrawal of this rejection is respectfully requested.

**II. Rejections under 35 U.S.C. § 102(a) and 102(b)**

The Office rejected claims 1-2, 11 and 13 under 35 U.S.C. § 102(b) as allegedly anticipated by Moutsatsos et al. (WO 99/11664); claims 1-2, 4, 11 and 13 under 35 U.S.C. § 102(b) as allegedly anticipated by Riew et al. (Calcif. Tissue Int. 63:357-360, 1998), in view of Caplan et al. (U.S. 5,855,619); and claims 1-2, 4, 11 and 13 under 35 U.S.C. § 102(a) as allegedly anticipated by Cheng et al. (Calif. Tissue Int. 68:87-94, 2001), in view of Caplan et al. These rejection is respectfully traversed for the reasons set forth below.

Anticipation under 102(a) or (b) requires that a single prior art reference disclose each and every element of the claim. *In re Spada*, 911 F.2d 705, 707, 15 U.S.P.Q.2d 1655 (Fed. Cir. 1990); *RCA Corp v. Applied Digital Data Sys., Inc.*, 730 F.2d 1440, 1444, 221 U.S.P.Q. 385, 388 (Fed. Cir. 1984). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir.

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1987); M.P.E.P. 2131. Furthermore, the Office has the initial burden of establishing a *prima facie* case of anticipation. *In re Wilder*, 429 F.2d 447, 450, 166 U.S.P.Q. 545, 548 (CCPA 1970).

Amended claim 1 is directed to a pharmaceutical composition for application at a biodegradable plate-containing site requiring new bone or cartilage formation in a subject. The composition comprises a plurality of bone marrow stromal cells (MSCs) and a pharmaceutically acceptable polymer, wherein the MSCs are isolated from the subject, are transduced *in vitro* after isolation from the subject with a replication-deficient viral vector comprising a DNA sequence encoding BMP-2 operably linked to a promoter, and are applied at the biodegradable plate-containing site. Claims 2, 11 and 13 are dependent on claim 1.

None of Moutsatsos et al., Riew et al., Cheng et al. or Caplan et al., teach or suggest a pharmaceutical composition for application at a biodegradable plate-containing site requiring new bone or cartilage formation in a subject. Moutsatsos et al. does not teach or disclose such a composition comprising a plurality of bone marrow stromal cells (MSCs) and a pharmaceutically acceptable polymer, wherein the MSCs are isolated from the subject, are transduced *in vitro* after isolation from the subject with a replication-deficient viral vector comprising a DNA sequence encoding BMP-2 operably linked to a promoter, and are applied at the biodegradable plate-containing site.

As such, the Office has not set forth a *prima facie* case of anticipation of claims 1-2, 11 and 13 in view of any of Moutsatsos et al.; Riew et al. in evidence of Caplan et al.; or Cheng et al. in evidence of Caplan et al., and reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(a) and § 102(b) are respectfully requested.

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In view of the above, it is respectfully submitted that the pending claims are in condition for allowance. The Examiner is encouraged to contact the undersigned with any questions or to otherwise expedite prosecution.

Respectfully Submitted,



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